

### **REMARKS**

In an office action mailed November 6, 2002, the Examiner has rejected claims 29, 31, 34, 35, and 37-44 under 35 USC §102(e), and claims 32, 33 and 36 under 35 USC §103. In response thereto, Applicants submit the above amendments and the following remarks.

By this amendment, claims 30-32 have been cancelled, and claim 29 has been amended. Accordingly, claims 29, and 33-45 are pending in the application.

### **The Invention**

The invention relates to a method for improving the benefits of a vaccination. Applicants have discovered a novel method for inducing or stimulating T-helper cell response in a human or an animal against at least one antigen.

According to the claimed method, a first vaccine composition comprising the antigen and a first vector is administered to the animal or human. Next, a second vaccine composition comprising the antigen and a second vector is administered. Finally, a third vaccine composition comprising the antigen and a third vector is administered. The first, second and third vectors are different from each other.

The claimed invention has the advantage that both humoral and cellular immunity can be obtained. Moreover, a T-helper cell response is capable of generating long term memory for both cellular and humoral immunity, therefore, improving the overall performance of the vaccination.

### **Rejections Under §102**

In the office action, claims 29, 31, 34, 35, and 37-44 have been rejected under §102(e) as being anticipated by U.S. Patent No. 6,210,663 to Ertl. According to the Examiner, Ertl discloses sequential immunization using a DNA plasmid vector followed by an adenovirus vector, which allegedly induces a Th1 response. Ertl also allegedly discloses adding an immune response modulator encoding sequence.

Claim 29 has been amended to include the substance of cancelled claims 30-32. Claim 29 is now directed to a three-step vaccination method in which all three vaccines utilize different vectors, and where the antigen is a lentivirus.

Ertl discloses a two step vaccination method for enhancing mucosal immunity. Ertl does not disclose a three step vaccination method against a lentivirus. Therefore, in view of the herein amendments to claim 29, Ertl cannot be found to anticipate the claims.

Accordingly, applicants respectfully request that the rejections under §102(e) based on Ertl be reconsidered and withdrawn.

### **Rejections Under §103**

Claims 32, 33 and 36 have been rejected under §103 as being unpatentable over Ertl. The Examiner recognizes that Ertl does not disclose a lentivirus antigen or antigen from an immune

impairing virus. However, the Examiner contends that because Ertl discusses HIV as a suitable virus target for the method disclosed, "it would have been obvious to choose one of the known HIV antigenic proteins as an obvious variation on the disclosed immunization method, for the purpose of inducing a desirable mucosal immune response directed against HIV." Page 2 of the office action. Applicants respectfully disagree.

As a result of the present invention, it has been unexpectedly discovered that a three-step vaccination protocol utilizing three different vectors, provides satisfactory protection against a lentivirus antigen. The examples provided in the present application are directed to simian immunodeficiency virus (SIV). It is well known that SIV closely resembles HIV, and both are lentiviruses.

Table 1, on page 20 of the application, demonstrates that subjects that received a two-step vaccination protocol with two different vectors (Groups B and C) did not obtain satisfactory protection against SIV. This is the method allegedly disclosed in Ertl.

Surprisingly, in the present invention, the subjects that received a three-step vaccination protocol with three different vectors (Group D) obtained satisfactory protection against SIV. This result was unexpected. Hence, the invention as a whole is not prima facie obvious in view of Ertl.

From reading Ertl, one of ordinary skill in the art would not be motivated to use the three step vaccination method of the present invention, to obtain satisfactory protection against a lentivirus such as, for example, SIV or HIV.

Ertl merely mentions HIV as an example of a sexually transmitted pathogen. Ertl does not teach how to induce or stimulate a T helper cell response to a lentivirus such as , for example, SIV or HIV. Ertl does not disclose or suggest a three-step vaccination protocol that utilizes three different vectors.

In order to establish a *prima facie* case of obviousness, one of the criteria to be met is that the prior art reference must teach or suggest all of the claim limitations. See MPEP §2142.

Applicants' have demonstrated the importance of utilizing a three step vaccination protocol that utilizes three different vectors. Applicants have also demonstrated the unexpected results obtained using the three step protocol for inducing immunity against a lentivirus. Upon reading the teachings Ertl, all of Applicants' claimed limitations are not taught or suggested. Therefore, based on the foregoing discussion, Applicants' claimed invention is not obvious over Ertl.

Claims 30 and 45 have been rejected under §103 as being unpatentable over Ertl in view of U.S. Patent No. 5,958,895 to Pachuk et al. The Examiner recognizes that Ertl does not disclose a third vector for administration. However, the Examiner contends that because Pachuk et al. disclose a nucleic acid vaccination method that utilizes a primary and first boost to induce Th1

response, and a second boost to induce a Th2 response, it would have been obvious to one of ordinary skill in the art to modify Ertl by administering a second boost designed for driving Th2 response. Applicants disagree.

Although the teachings of Pachuk et al. are appreciated, Pachuk et al. do not disclose or suggest utilizing a three step vaccination protocol that utilizes three different vectors, to obtain an immune response to a lentivirus.

In the office action, the Examiner suggests that because Ertl discloses avoiding an anti-viral immune response to the boosting vector by using another virus as the carrier portion of the booster, it would have been obvious to use a different vector for the second booster. See page 3 of the office action. Applicants disagree.

Pachuk is exclusively concerned with vaccinations against Herpes Simplex Virus (HSV). HSV is not a lentivirus. There is absolutely no mention in Pachuk concerning problems with, or a desire to avoid, anti-viral immune response to the boosting vector.

Similarly, there is absolutely no mention in Ertl concerning a desire to induce a Th2 response. As discussed above, Ertl is exclusively concerned with inducing mucosal immunity.

In the opinion of Applicant's representative, the examiner has engaged in a classical example of picking and choosing isolated disclosures in the prior art, and then using hindsight, to

solve the problem first solved by the present inventor. Applicant respectfully requests the examiner to reconsider what a person having ordinary skill in the art would have learned from the combination of the Ertl and Pachuk references without the benefit of the present application.

Applicants have surprisingly discovered that the three step approach of the claimed invention provides unexpectedly superior results compared to a two step approach, as disclosed in Ertl.

As discussed above, in order to establish a *prima facie* case of obviousness, one of the criteria to be met is that the prior art references, when combined, must teach or suggest all of the claim limitations. See MPEP §2142.

Applicants' have demonstrated the importance of utilizing a three step vaccination protocol that utilizes three different vectors, especially to obtain immunity to a lentivirus. Upon combining the teachings Ertl and Pachuk, all of Applicants' claimed limitations are not taught or suggested. Therefore, based on the foregoing discussion, Applicants' claimed invention is not obvious over Ertl in view of Pachuk.

Accordingly, Applicants respectfully request that the above rejections under §103 based on Ertl, and Ertl in view of Pachuk, be reconsidered and withdrawn.

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Page 9 of 10

In light of the foregoing amendments and remarks, Applicants respectfully submit that the application is now in condition for allowance. If the Examiner believes a telephone discussion with the Applicant's representative would be of assistance, she is invited to contact the undersigned at her convenience.

Respectfully submitted,



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Lauren T. Emr  
Attorney for Applicant  
Registration No.: 46,139

HOFFMANN & BARON, LLP  
6900 Jericho Turnpike  
Syosset, New York 11791  
(516) 822-3550  
LTE:jlw

**VERSION OF AMENDMENT WITH MARKINGS TO SHOW CHANGES MADE**

**In the claims:**

Please cancel claims 30-32;

Please amend claim 29 as follows:

29. A method for inducing or stimulating a T-helper cell response in a human or animal against at least one antigen comprising the steps of:

i. administering a first vaccine composition comprising said antigen and a first vector;  
and

ii. administering a second vaccine composition comprising said antigen and a second vector; and

iii. administering a third vaccine composition comprising said antigen and a third vector;

wherein the first, ~~and~~ second and third vectors are different from each other; ~~and~~

wherein the first, ~~and~~ second and third vaccine compositions are administered sequentially to the animal or human;

wherein the antigen is an antigen of a virus; and

wherein the virus is a lentivirus.